

What is claimed is:

1. A method of regenerating a mesenchymally-derived tissue, comprising contacting said tissue with a composition comprising an isolated adult mesenchymal stem cell, said mesenchymal stem cell comprising an exogenous nucleic acid encoding an akt gene.
2. The method of claim 1, wherein said tissue is selected from the group consisting of connective tissue, epithelial tissue, nervous tissue and muscle tissue.
3. The method of claim 1, wherein said tissue is selected from the group consisting of myocardial, brain, spinal cord, bone, cartilage, liver, muscle, lung, vascular, and adipose tissue.
4. The method of claim 2, wherein said muscle tissue comprises skeletal muscle.
5. The method of claim 2, wherein said muscle tissue comprises smooth muscle.
6. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding a homing molecule.
7. The method of claim 6, wherein said homing molecule is selected from the group consisting of a chemokine receptor, an interleukin receptor, an estrogen receptor, an integrin receptor
8. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding a hormone.
9. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding an angiogenic factor.
10. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding a bone morphogenetic protein.
11. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding an extracellular matrix protein.

12. The method of claim 1, wherein said mesenchymal stem cell further comprises an exogenous nucleic acid encoding a cytokine or growth factor.

13. A composition comprising an apoptosis-resistant primary stem cell, said stem cell comprising an exogenous akt gene, wherein apoptosis of said cell is reduced by at least 10% compared to a primary mesenchymal stem cell lacking said akt gene.

14. The composition of claim 13, wherein said stem cell is an adult bone-marrow derived mesenchymal cell.

15. The composition of claim 13, wherein said apoptosis is reduced by at least 50%.

16. The composition of claim 13, wherein said apoptosis is reduced by at least 2-fold.

17. The composition of claim 13, wherein said apoptosis is reduced by at least 5-fold.

18. The composition of claim 13, wherein said apoptosis is reduced by at least 10-fold.

19. The composition of claim 13, wherein said stem cell is non-tumor forming.

20. The composition of claim 13, wherein said stem cell further comprises a homing receptor.

21. A method of regenerating an injured myocardial tissue, said method comprising contacting said tissue with the composition comprising an isolated adult recombinant mesenchymal stem cell (rMSC), said rMSC comprising an exogenous nucleic acid operably linked to a promoter, wherein said nucleic acid expresses a therapeutically effective amount of an anti-apoptotic gene.

22. The method of claim 21 wherein said mesenchymal stem cells are administered to an individual to regenerate or repair cardiac muscle that has been damaged through disease.

23. The method of claim 22 wherein said mesenchymal stem cells are administered to an individual who has suffered myocardial infarction.

24. The method of claim 22 wherein said mesenchymal stem cells are administered directly to the heart.

25. The method of claim 22 wherein said mesenchymal stem cells are administered systemically.

26. The method of claim 25 wherein said mesenchymal stem cells are administered by injection.

27. The method of claim 22 wherein said mesenchymal stem cells are human.

28. The method of claim 27 wherein said mesenchymal stem cells are administered to an individual who has suffered myocardial infarction.

29. The method of claim 28 wherein said mesenchymal stem cells are administered directly to the heart.

30. The method of claim 28 wherein said mesenchymal stem cells are administered systemically.

31. A method of regenerating myocardial tissue, said method comprising contacting said tissue with the composition comprising an isolated adult recombinant mesenchymal stem cell (rMSC), said rMSC comprising an exogenous nucleic acid operably linked to a promoter, wherein said nucleic acid expresses a therapeutically effective amount of a cell protective polypeptide, wherein the expression of said polypeptide is induced by a triggering agent or condition.

32. The method of claim 31, wherein the condition is hypoxia or oxidative stress.

33. The method of claim 31, wherein the agent is an antibiotic

34. The method of claim 33, wherein said antibiotic is tetracycline.

35. The method of claim 31, wherein the agent is an immunosuppressive.

36. The method of claim 35, wherein said immunosuppressive is rapamycin.

37. The method of claim 31, wherein the agent is a hormone receptor antagonist.

38. The method of claim 37, wherein said hormone receptor antagonist is mifepristone.

39. The method of claim 31, wherein the cell protective polypeptide is selected from the group consisting of an antioxidant enzyme protein, a heat shock protein, an anti-inflammatory protein, a survival protein, an anti-apoptotic protein, a coronary vessel tone protein, a pro-angiogenic protein, a contractility protein, a plaque stabilization protein, a thromboprotection protein, a blood pressure protein and a vascular cell proliferation protein.

40. The method of claim 31, wherein the subject is at risk of developing a condition characterized by aberrant cell damage.

41. The method of claim 31, wherein said aberrant cell damage is apoptotic cell death.

42. The method of claim 31, wherein said subject is at risk of developing stroke, myocardial infarction, chronic coronary ischemia, arteriosclerosis, congestive heart failure, dilated cardiomyopathy, restenosis, coronary artery disease, heart failure, arrhythmia, angina, atherosclerosis, hypertension, renal failure, kidney ischemia or myocardial hypertrophy.

43. The method of claim 21, wherein at least 20% of said injured myocardial tissue is regenerated.

44. A composition comprising an isolated mesenchymal stem cell comprising an exogenous nucleic acid encoding a tissue protective polypeptide, a oxygen sensitive regulatory element and a cell targeting element, wherein the expression of said polypeptide is regulated by said regulatory element

45. The composition of claim 44, wherein said oxygen sensitive regulatory element is a hypoxia response element.

46. The composition of claim 44, wherein said oxygen sensitive regulatory element is a oxidative stress response element.

47. The composition of claim 46, wherein said oxidative stress response element is a peroxidase promoter.

48. The composition of claim 44, wherein said cell targeting element is selected from the group consisting of  $\alpha$ -MHC, myosin light chain-2, troponin T.

49. The composition of claim 44, wherein the composition comprises vector selected from the group consisting of an adeno-associated virus vector, lentivirus vector retrovirus vector.

50. The composition of claim 44, wherein the composition comprises an adeno-associated virus vector.

51. A method of inhibiting apoptosis of grafted cells in a mammal, said method comprising administering to said mammal a composition comprising an isolated mesenchymal stem cell comprising an exogenous nucleic acid encoding a polypeptide selected from the group consisting of: an extracellular superoxide dismutase polypeptide, a heme oxygenase polypeptide, and an Akt polypeptide, wherein said mammal is suffering from or at risk of developing a cardiac disorder.

52. The method of claim 51, wherein said cardiac disorder is selected from the group consisting of chronic coronary ischemia, arteriosclerosis, congestive heart failure, angina, atherosclerosis, and myocardial hypertrophy.

53. The method of claim 51, wherein said composition comprises an adeno-associated virus vector.

54. The method of claim 51, wherein the human heme oxygenase-1 nucleic acid is operatively linked to a promoter.

55. The method of claim 54, wherein said promoter is a human cytomegalovirus immediate early promoter.

56. The method of claim 51, wherein said human heme oxygenase-1 nucleic acid is operatively linked to a bovine growth hormone polyadenylation signal.

57. The method of claim 56, wherein said bovine growth hormone polyadenylation signal is flanked by the adeno-associated viral inverted terminal repeats.

58. The method of claim 51, wherein said composition is administered at a dose sufficient to increase survival of engrafted mesenchymal stem cell oxidative stress-induced cardiomyocyte cell death.

59. A method of increasing post-transplantation survival of engrafted cells in a mammal in a mammal, said method comprising administering to said mammal a composition comprising an isolated mesenchymal stem cell comprising an exogenous nucleic acid encoding a polypeptide selected from the group consisting of: an extracellular superoxide dismutase polypeptide, a heme oxygenase polypeptide, and an Akt polypeptide, thereby increasing survival of the engrafted cells.

60. The method of claim 59, mammal is at risk of a cardiac disorder.

61. The method of claim 59, wherein said cardiac disorder is selected from the group consisting of myocardial infarction, chronic coronary ischemia, arteriosclerosis, congestive heart failure, angina, atherosclerosis, and myocardial hypertrophy.

62. The method of claim 59, wherein said composition comprises an adeno-associated virus vector.

63. The method of claim 59, wherein the extracellular superoxide dismutase nucleic acid is operatively linked to a promoter.

64. The method of claim 63, wherein said promoter is a human cytomegalovirus immediate early promoter.

65. The method of claim 59, wherein said extracellular superoxide dismutase polypeptide nucleic acid is operatively linked to a bovine growth hormone polyadenylation signal.

66. The method of claim 65, wherein said bovine growth hormone polyadenylation signal is flanked by the adeno-associated viral inverted terminal repeats.

67. The method of claim 59, wherein said composition is administered at a dose sufficient to inhibit oxidative stress-induced cardiomyocyte cell death.

68. A method of treating a cardiac disorder, comprising identifying a mammal suffering from or at risk of developing said disorder and administering to said mammal a composition comprising an isolated mesenchymal stem cell comprising an exogenous nucleic acid expressing therapeutic amounts of a polypeptide selected from the group consisting of: an extracellular superoxide dismutase polypeptide, a heme oxygenase polypeptide, and an Akt polypeptide.

69. The method of claim 68, wherein said composition comprises an adeno-associated virus vector.

70. The method of claim 69, wherein the extracellular superoxide dismutase polypeptide nucleic acid is operatively linked to a promoter.

71. The method of claim 70, wherein said promoter is a human cytomegalovirus immediate early promoter.

72. The method of claim 68, wherein said extracellular superoxide dismutase nucleic acid is operatively linked to a bovine growth hormone polyadenylation signal.

73. The method of claim 72, wherein said bovine growth hormone polyadenylation signal is flanked by the adeno-associated viral inverted terminal repeats.

74. The method of claim 68, wherein said cardiac disorder is selected from the group consisting of myocardial infarction, chronic coronary ischemia, arteriosclerosis, congestive heart failure, dilated cardiomyopathy, restenosis, coronary artery disease, heart failure, arrhythmia, angina, atherosclerosis, hypertension, renal failure, kidney ischemia or myocardial hypertrophy, and stroke.

75. A cardioprotective agent comprising a recombinant adeno-associated viral vector comprising nucleotide encoding a extracellular superoxide dismutase polypeptide operatively linked to a human cytomegalovirus immediate early promoter.

76. The cardioprotective agent of claim 75, further comprising a bovine growth hormone polyadenylation signal.

77. The cardioprotective agent of claim 76, wherein said bovine growth hormone polyadenylation signal is flanked by the adeno-associated viral inverted terminal repeats.

78. A method for reducing scar formation in infarcted heart tissue, said method comprising contacting said tissue with the composition comprising an isolated adult recombinant mesenchymal stem cell (rMSC), said rMSC comprising an exogenous nucleic acid operably linked to a promoter, wherein said nucleic acid expresses a therapeutically effective amount of an anti-apoptotic gene.

79. A composition comprising an isolated adult recombinant mesenchymal stem cell (rMSC), said rMSC comprising an exogenous nucleic acid operably linked to a promoter, wherein said nucleic acid expresses a therapeutically effective amount of an anti-apoptotic gene.

80. The composition of claim 79, wherein the anti-apoptotic gene is selected from the group consisting of an Akt gene, an extracellular superoxide dismutase (ecSOD) polypeptide and a heme oxygenase gene.

81. A method of enhancing migration of a stem cell to an injured tissue, comprising increasing the amount of a stem cell polypeptide on the surface of said stem cell, wherein said stem cell polypeptide is selected from the group consisting of CXCR4, IL-6RA, IL-6ST, CCR2, Sele1, Itgal/b2, Itgam/b2, Itga4/b1, Itga8/b1, Itga6/b1, and Itga9/b1.

82. The method of claim 81, wherein said cell is a bone marrow-derived stem cell.

83. The method of claim 81, wherein said cell is a mesenchymal stem cell.

84. The method of claim 81, wherein said method comprises introducing into said stem cell a nucleic acid encoding said receptor.

85. A method of enhancing engraftment of a stem cell to an injured tissue, comprising increasing the amount of an injury-associated polypeptide in said injured tissue, wherein said injury-associated polypeptide is selected from the group consisting of SDF1, IL-6, CCL2, Sele, ICAM-1, VCAM-1, FN, LN, and Tnc.

86. The method of claim 85, wherein said injured tissue is cardiac tissue.

87. The method of 85, wherein said injured tissue is ischemic myocardial tissue.

88. The method of claim 85, wherein said method comprises contacting said injured tissue with a nucleic acid encoding said injury-associated polypeptide.

89. The method of claim 85, wherein said method comprises contacting said injured tissue with said injury-associated polypeptide.

90. The method of claim 85, wherein said method comprises injecting said injury-associated polypeptide or a nucleic acid encoding said polypeptide directly into the myocardium.